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10/083,413	02/27/2002	Avraham J. Domb	Q63391	7369

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EXAMINER
FLOOD, MICHELE C

ART UNIT	PAPER NUMBER
1654	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/083,413	Applicant(s) Domb et al.
	Examiner Michele Flood	Art Unit 1654

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 17, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above, claim(s) *27-34* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-12, 15-17, 19, 22, 23, and 26* is/are rejected.

7) ☒ Claim(s) *13, 14, 18, 20, 21, 24, and 25* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on April 17, 2003.

Claims 1-26 are under examination.

The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment

Claim Rejections - 35 USC § 102

1. Claims 1, 4, 5, 15-17, 22, 23 and 26 as amended remain rejected under 35 U.S.C. 102(e) as being anticipated by Tapolsky et al. (A). The rejection stands for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant argues that Tapolsky does not teach the claimed invention. However, this is not persuasive because Tapolsky teaches a solid, self-bioadhesive composition for topical application that adheres to the oral mucosal tissue comprising a therapeutically effective amount of at least one herbal active agent (e.g., thymol which is obtained from thyme oil and eugenol which is obtained from clove oil) and a pharmaceutically acceptable solid bioadhesive carrier in an amount from about 5-95% by weight of the total composition, and wherein the bioadhesive comprises hydroxyethyl cellulose, polyacrylic acid, and sodium carboxymethyl cellulose. See claims 1, 10 and 11; and Column 6, lines 27-37. In Column 5, lines 31-58, Tapolsky teaches that the bioadhesive composition is in the form of a disk having two layers: an adhesive layer and a non-

adhesive backing layer. The adhesive layer comprises a film forming polymer which may be crosslinked (see Column 5, lines 61-67; Column 6; and Column 7, lines 1-12). In Column 5, lines 16-30, Tapolsky teaches that the residence times which may be achieved for the referenced composition include 30 minutes to about 3 or about 4 hours. A preferred residence time for effective drug delivery is about 1 to 2 hours. In Column 7, line 13 bridging Column 8, lines 1-12, examples of pharmaceuticals which may be incorporated into the making of the referenced composition are taught, including inflammatory analgesic agents, steroidal anti-inflammatory agents, antihistamines, local anesthetics, bactericides and disinfectants, vasoconstrictors, hemostatics, chemotherapeutic agents, antibiotics, keratolytics, cauterizing agents, and antiviral drugs. In Column 8, lines 25-32, Tapolsky teaches that the thickness of the composition may vary, depending on the thickness of each of the layers. Preferably, the bilayer thickness ranges from 0.05 to 1 mm. In Column 12, lines 66-67, disk having a ½ inch (12.7 mm) is taught by Tapolsky.

Applicant's main arguments are directed to the idea that the Tapolsky' composition differs from the instantly claimed composition because "No herbals or homeopathics were mentioned or suggested in Tapolsky" and that the method of making the referenced composition are different from the method of making the instantly claimed compositions. However, Applicant's arguments are neither persuasive nor commensurate in scope to the limitations of the claimed invention. Indeed, Tapolsky does teach incorporating herbal active ingredients into the making of his compositions. For instance, Tapolsky teaches thymol and eugenol as a

pharmaceutical, i.e., bioactive agent, comprising the referenced composition. See Claims 1, 10 and 11. Please note that thymol is a bioactive agent obtained from thyme oil and eugenol is a bioactive agent obtained from clove oil.

Hence, the cited reference is deemed to anticipate the claimed subject matter.

Claims 1, 4-7, 15-17, 22 and 23 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by Roreger et al. (B) with evidence provided by Lawless (U). The rejection stands for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant argues that Roreger fails to anticipate the claimed invention. However, this is not persuasive because Roreger teaches a hydrophilic, insoluble gel film for topical application that adheres to oral mucosal tissue comprising a therapeutically effective amount of at least one herbal, 0.05 to 30%-weight of at least one anionic water-soluble polymer, and 0.05 to 30%-weight of at least one cationic water-soluble polymer. In Column 2, lines 32 to Column 3, lines 1-15, Roreger teaches polymers which can be used in the making of the referenced composition. In Column 10, lines 31-64, the gel film is taught as a carrier of therapeutics to the mouth or the mucous area of the mouth for the treatment of diseases and inflammation. Roreger teaches, in Column 10, lines 64 bridging Column 11, and Column 12, lines 1-27, various therapeutic agents (e.g., anesthetics, antiseptics, astringents, antibiotics, herbal extracts, and herbal essential oils). In Example 21, an insoluble gel film comprising myrrh tincture and sage tincture for application and

adherence to the mucous membrane of the mouth is taught (see Column 15, lines 52 to Column 16, lines 1-4).

The reference is deemed to anticipate the claimed subject matter.

Claim Rejections - 35 USC § 103

2. Claims 1-5, 15-17, 22, 23 and 26 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over Tapolsky et al. (A). The rejection stands for the reasons set forth in the previous office action and set forth below.

Applicant's arguments have been fully considered but they are not deemed persuasive because the cited reference provides the suggestions and motivation to the claimed invention.

Applicant argues "that for at least the same reasons that Tapolsky does not anticipate the claimed invention, Tapolsky doe not render Applicants' invention therefrom". However, this is not persuasive. The teachings of Tapolsky were relied upon for the reasons set forth above. Although Tapolsky does not expressly teach a solid, self-bioadhesive composition comprising the instantly claimed measurements, the Office maintains that it would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust the thickness and the diameter of the composition taught by Tapolsky because Tapolsky teaches the requisite ingredients and amounts of ingredients, the residence times for effective drug delivery, and process steps for making the layers of the referenced composition, which can be used in the making of a disc having varying measurements of thickness and diameter. At the time the invention was made, one of

ordinary skill in the art would have been motivated and one of ordinary skill in the art would have had a reasonable expectation to modify the measurements of the disc-shaped composition taught by Tapolsky to the instantly claimed measurements because Tapolsky teaches, in Column 8, lines 25-30, "The thickness of each layer may vary from 10 to 90% of the overall thickness of the bilayer device, and preferably varies from 30 to 60%." Thus, it would have been merely a matter of judicious selection to one of ordinary skill in the art at the time the invention was made to modify the combinations of the ingredients, the amounts of the ingredients, and the process steps for making the layers of the referenced composition in the making of the claimed composition because it would have been well in the purview of one of ordinary skill in the art practicing the invention to select result-effect amounts and degrees of thickness of the claimed ingredients to provide a composition with the claimed functional effect and claimed physical properties. Hence, it appears that the claimed invention is no more than the routine optimization of result effect variables.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claims 1-11, 15-17, 19, 22, 23 and 26 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over Tapolsky et al. (A) in view of Iyer et al. (E) and Friedman et al. (D, US 6,197,305) with evidence provided by Lawless (U). The rejection stands for the reasons set forth in the previous office action and set forth below.

Applicant's arguments have been fully considered but they are not deemed persuasive because the cited references provide the suggestions and motivation to the claimed invention.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the primary reference of Tapolsky was relied upon for the reasons set forth above. Because Tapolsky teaches the claimed invention except for wherein the herbal active agent or homeopathic active agent is at least one selected from the Markush group recited in Claim 6, wherein the herbal active agent is at least one essential oil selected from the Markush group recited in Claim 7, wherein the herbal active agent comprises at least one monoterpene with three unsaturations, wherein the herbal active agent is an essential oil and the essential oil is a natural or synthetic mixture consisting of and at least one of myrcene, a-pinene, b-pinene, and sabinene characterized in that at least 60% by weight of the mixture is limonene, and wherein said monoterpenes with

three unsaturations is of citrus oil selected from the group consisting of lemon, pomella and citron, the secondary references of Iyer and Friedman with evidence provided by Lawless were relied upon because Iyer teaches antimicrobial compositions which can be used in the making of oral compositions and Friedman teaches antifungal compositions which can be used in the making of oral compositions. Firstly, Iyer teaches antimicrobial compositions comprising at least two antimicrobial agents, agent A and agent B, which exhibit reduce MIC values relative to the MIC for the agents making up the combination measured alone. For example, in Column 3, lines 11-26, Iyer teaches that agent A and agent B are selected from the group consisting of berberine, cedarwood oil, chloramphenicol, citral, citronella oil, cocamidopropyl dimethylglycine, *Glycyrrhiza glabra* extract, hinokitol, juicy fruit basil oil, juniper berries oil, lemon basil oil, lemon oil, and *Rosmarinus officinalis* oil. The compositions taught by Iyer are useful as therapeutic agents such as in oral hygiene products. Secondly, Friedman teaches a combination of an herbal extract and an essential oil which exerts prolonged antifungal activity on mucosal membranes. The herbal extracts include material selected from the group consisting of Plantago, Hypericum, Echinacea, Baptisia, Calendula, Myrrh, Phytolocca, Salvia, Catechu black, Coneflower, Krameria, Tsuga, Rosmarinus, Styrax, Crataegus, Glycerrhiza, Angelica, Krameria, Matricaria, Mallow, Propolis (beehive material), and Sage; and the essential oils are selected from cinnamon oil, cajeput oil, citronella oil, eucalyptus oil, fennel oil, geranium oil, lavender oil, lemon oil, spearmint oil, myrte oil, oregano oil, pine oil, rosemary oil, sarriette oil, thyme oil, and tea-tree oil (see Column 1, lines 6-10; Column 2, lines 38-59; and claims). In Column 5, lines 9-39, Friedman

further teaches that the herbal extracts are in the form of a tincture of botanical materials. In Figures 1 and 2, Friedman shows that the referenced compositions have prolonged activity against *Aspergillus niger* and *Candida albicans*. In Column 4, lines 18-37, Friedman teaches that the compositions can be used to combat fungal infection of mucosal organs and the oral cavity. At the time the invention was made, one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to add the instantly claimed ingredients having the instantly claimed biochemical properties to the composition taught by Tapolsky to provide the claimed invention because Iyer teaches that the antimicrobial compositions of his invention can be used in the making of therapeutic oral hygiene products for growth control of bacteria, such as *Actinomyces viscosus, Campylobacter rectus, Fusobacterium nucleatum, Porphyromonas gingivalis, Streptococcus mutans* and *Streptococcus mutans* (see Column 3, lines 28-38 and 47-51); and Friedman teaches that the compositions of his invention have strong antibacterial activity and anti-inflammatory activity in addition to its antifungal activity, can be used in the making of oral products, and can be used in the treatment of disease conditions such as *Herpes zoster* and *Herpes simplex* infections, dental ulcers, stomatitis, aphthous ulcers, and abscesses (see Column 4, lines 31-37; Column 8, lines 36-42; Column 9, lines 66-67 to Column 10, lines 1-4; and Column 10, lines 30-51). One of ordinary skill in the art at the time the invention was made would have been further motivated and one would have had a high expectation of success to add the antimicrobial compositions taught by Iyer to the bioadhesive composition taught by Tapolsky to provide the claimed invention because Iyer teaches in Table 14

that the combination of the essential oil of lemon (which comprises 70% limonene, myrcene, pinenes and sabinene, as evidenced by the teaching of Lawless) in combination with an antimicrobial Agent B results in a significant decrease in the MIC value against various microorganisms which cause oral or periodontal disease. Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add any of the claimed ingredients in the making of the claimed methods because it is well known that its *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten,* 459 F. 2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi,* 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett,* 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

Thus, with Tapolsky providing the motivation to use a solid, self-bioadhesive composition as a topical application that adheres to oral mucosal that comprises a therapeutically effective amount of at least one herbal active agent and a pharmaceutically acceptable solid bioadhesive carrier in an amount from about 40 to 99 percent based on the weight of the whole composition, and with Iyer suggesting the use of plant essential oils as therapeutic agents for use in oral hygiene products, and finally with Friedman teaching that combining an herbal extract and an essential oil which exerts a prolonged antifungal activity on mucosal membranes, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the instantly

claimed old and well-known ingredients to provide a composition for the use as a composition for application to a mucous membrane as suggested by the cited references. As each of the references clearly indicate that the various proportions and amounts of the ingredients used in the claimed composition or the claimed composition/pharmaceutical combinations are result variables, they would have been routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by that reference. Therefore, the invention as a whole was clearly *prima facie* obvious in the absence to the contrary.

Claims 1-6, 12, 15-17, 22, 23 and 26 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over Tapolsky et al. (A) and Friedman et al. (D, US 6,197,6305) in view of Shuch et al. (F). The rejection stands for the reasons set forth in the previous office action and set forth below.

Applicant's arguments have been fully considered but they are not deemed persuasive because the cited references provide the suggestions and motivation to the claimed invention.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this

case, the primary reference of Tapolsky was relied upon for the reasons set forth above. Because Tapolsky does not teach a solid, self-bioadhesive for topical application comprising herb tincture active agents selected from the recited Markush group of Claim 6, and further comprising a salt selected from the group consisting of $MgBr_2$, NaCl, KCL and mixtures thereof the secondary references of Friedman and Shuch were relied upon because Friedman teaches antifungal compositions comprising botanical tinctures which can be used in the making of therapeutic oral compositions and Shuch teaches compositions comprising homeopathic salts and herbal botanicals which can be used in the making of therapeutic oral compositions. Firstly, Friedman teaches a combination of an herbal extract and an essential oil which exerts prolonged antifungal activity on mucosal membranes. The herbal extracts include material selected from the group consisting of Plantago, Hypericum, Echinacea, Baptisia, Calendula, Myrrh, Phytolocca, Salvia, Catechu black, Coneflower, Krameria, Tsuga, Rosmarinus, Styrax, Crataegus, Glycerrhiza, Angelica, Krameria, Matricaria, Mallow, Propolis (beehive material), and Sage; and the essential oils are selected from cinnamon oil, cajeput oil, citronella oil, eucalyptus oil, fennel oil, geranium oil, lavender oil, lemon oil, spearmint oil, myrte oil, oregano oil, pine oil, rosemary oil, sarriette oil, thyme oil, and tea-tree oil (see Column 1, lines 6-10; Column 2, lines 38-59; and claims). In Column 5, lines 9-39, Friedman further teaches that the herbal extracts are in the form of a tincture of botanical materials. In Figures 1 and 2, Friedman shows that the referenced compositions have prolonged activity against *Aspergillus niger* and *Candida albicans*. In Column 4, lines 18-37, Friedman teaches that the compositions can be used to combat fungal infection of mucosal organs and the

oral cavity. Secondly, Shuch teaches a biologically absorbable dental composition comprising Vitamin C to promote healing of the mouth from gum disease and to reduce plaque build-up on the teeth; and coenzyme A-10 (ubiquinone) to enhance gum health. Other active agents comprising the composition taught by Shuch include Vitamin E; herbal extracts, e.g., Propolis, Echinacea, grape seed extracts, cranberry extract, stevia, tangerine oil, and lemon oil; and homeopathic tissue salts comprising potassium chloride and sodium chloride. See Column 2, lines 40-67, Column 3, and Column 4, lines 1-42. The formulation may be in the form of a dental prophylaxis paste (see Column 6, lines 64-67; and Examples 9-13, especially Examples 12 and 13, which comprise homeopathic salts).

Thus, with Tapolsky providing the motivation to use a solid, self-bioadhesive composition as a topical application that adheres to oral mucosal that comprises a therapeutically effective amount of at least one herbal active agent and a pharmaceutically acceptable solid bioadhesive carrier in an amount from about 40 to 99 percent based on the weight of the whole composition, and with Friedman providing a combination of an herbal extract and an essential oil which exerts prolonged antifungal activity on mucosal membranes, and with Shuch teaching adsorbale oral compositions comprising herbal extracts and homeopathic salts to promote healthy gum tissues, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the instantly claimed old and well-known ingredients to provide a composition for the use as a composition for application to a mucous membrane as suggested by the cited references. As each of the references clearly indicate that the various proportions and amounts of the

ingredients used in the claimed composition or the claimed composition/pharmaceutical combinations are result variables, they would have been routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by that reference. Therefore, the invention as a whole was clearly *prima facie* obvious in the absence to the contrary.

Although not rising to the level of uncertainty, there is an apparent typographical error in Claim 6, line 6. Applicant may overcome the rejection by capitalizing the "h" in "hydratis".

Claim 19 recites the phrase "wherein the herbal active agent consists of a mixture of natural or synthetic monoterpenes with three unsaturations selected from the group consisting of limonene, myrcene, pinenes, sabinene, and terpinene". It is noted that not all of the recited herbal active agents are monoterpenes with three unsaturations. As drafted, Claim 19 recites only one monoterpene with three unsaturations, namely "myrcene".

Allowable Subject Matter

3. Claims 13, 14, 18, 20, 21, 24 and 25 would be allowable if rewritten to overcome the rejections set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is (703) 308-9432. The examiner can normally be reached on Monday through Friday from 7:15 am to 3:45 pm. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196 or the Supervisory Patent Examiner, Brenda Brumback whose telephone number is (703) 306-3220.

MCF

June 25, 2003

CHRISTOPHER R. TATE
PRIMARY EXAMINER